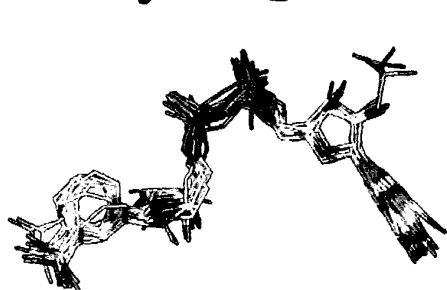
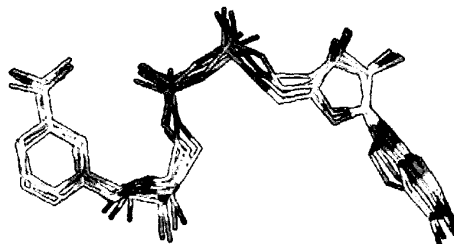


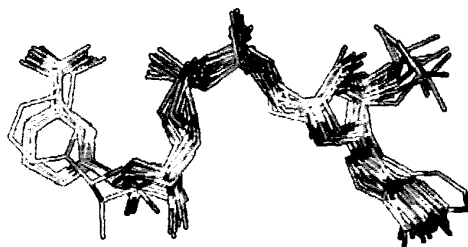
Dehydrogenase Pharmacoclusters



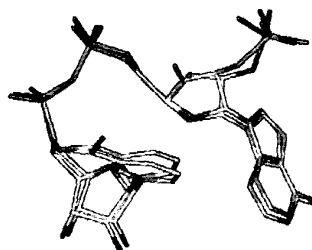
Pharmacocluster 1



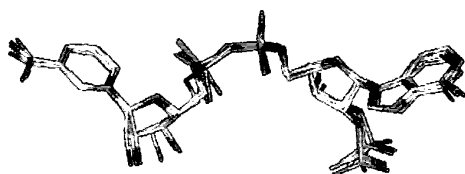
Pharmacocluster 2



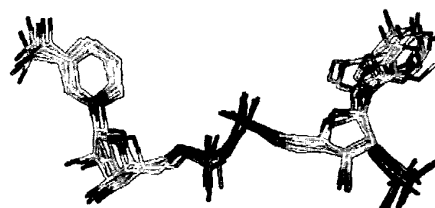
Pharmacocluster 3



Pharmacocluster 4



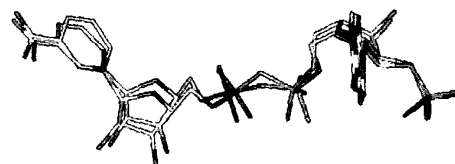
Pharmacocluster 5



Pharmacocluster 6



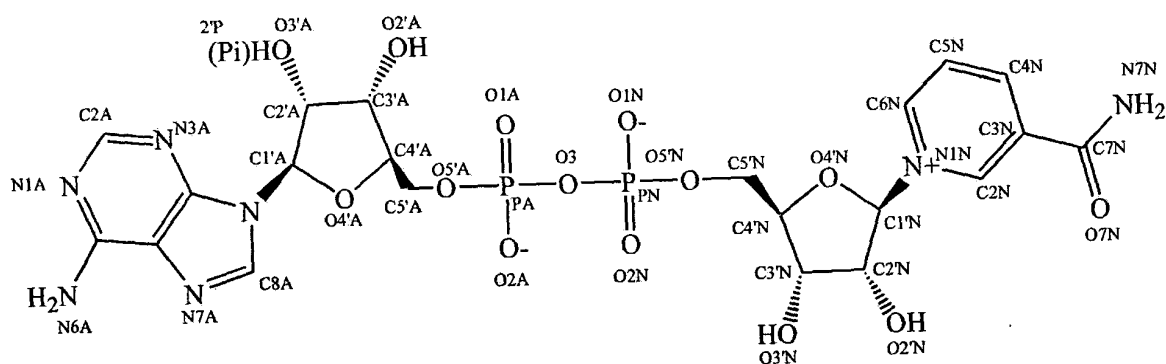
Pharmacocluster 7



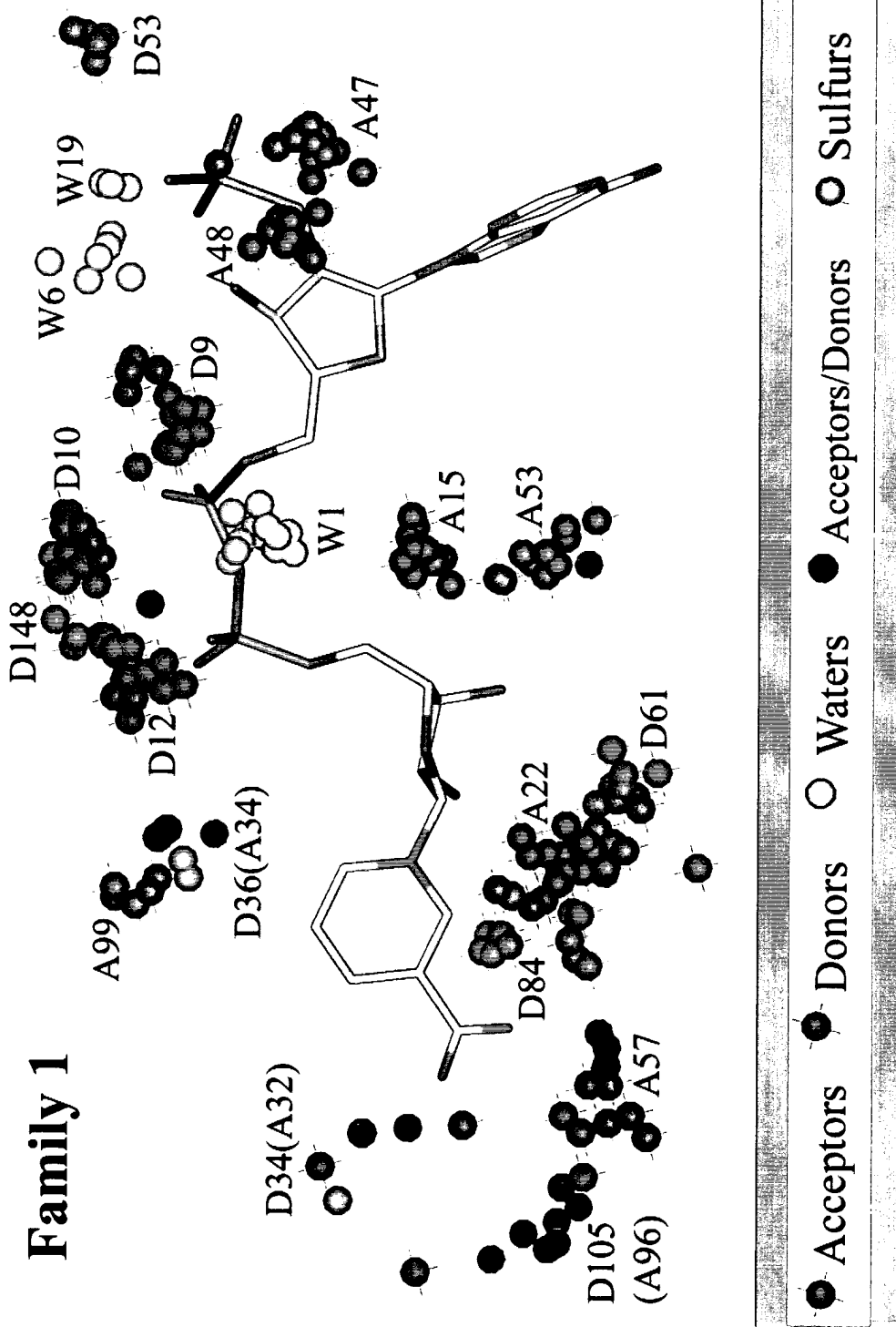
Pharmacocluster 8

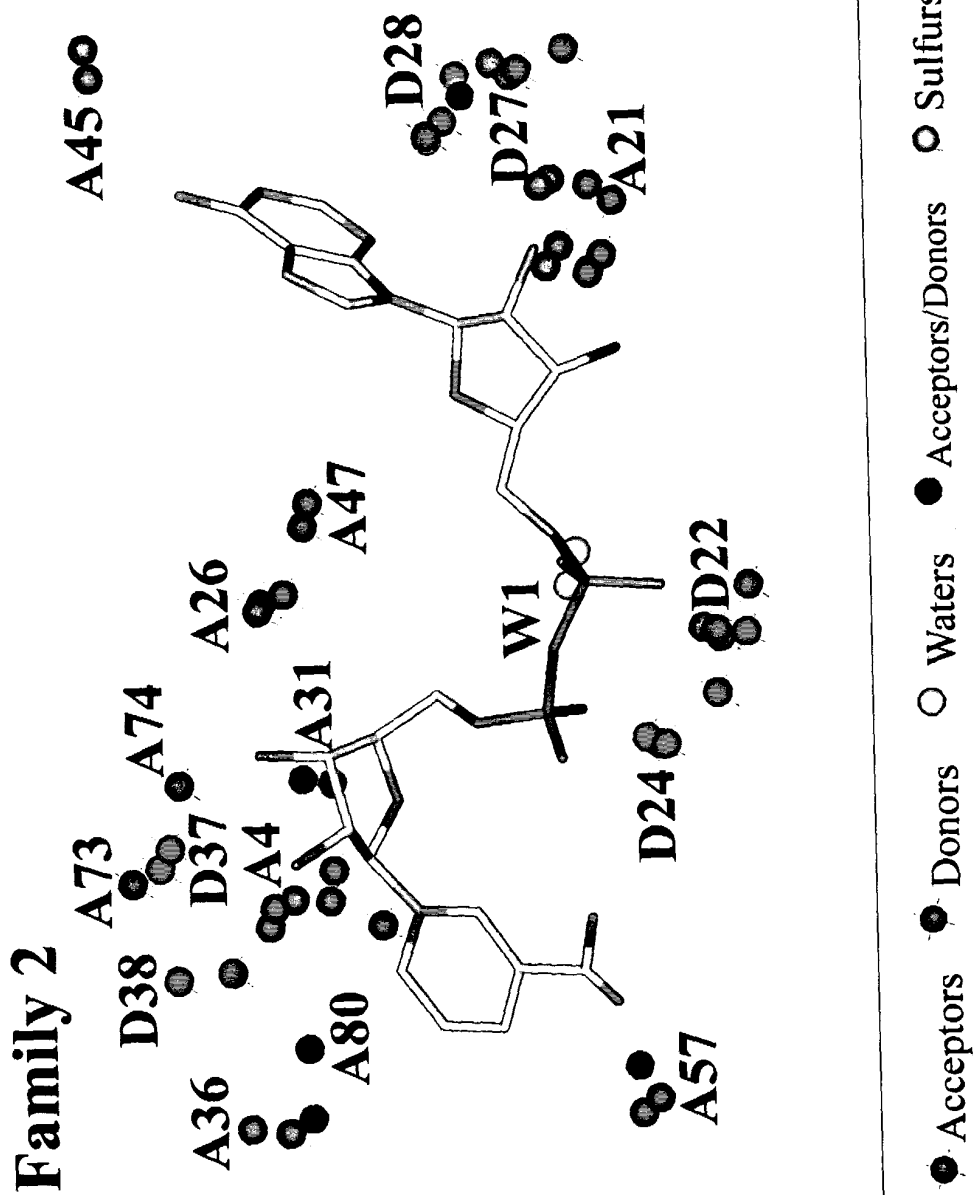
[illegible]

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Figure 2



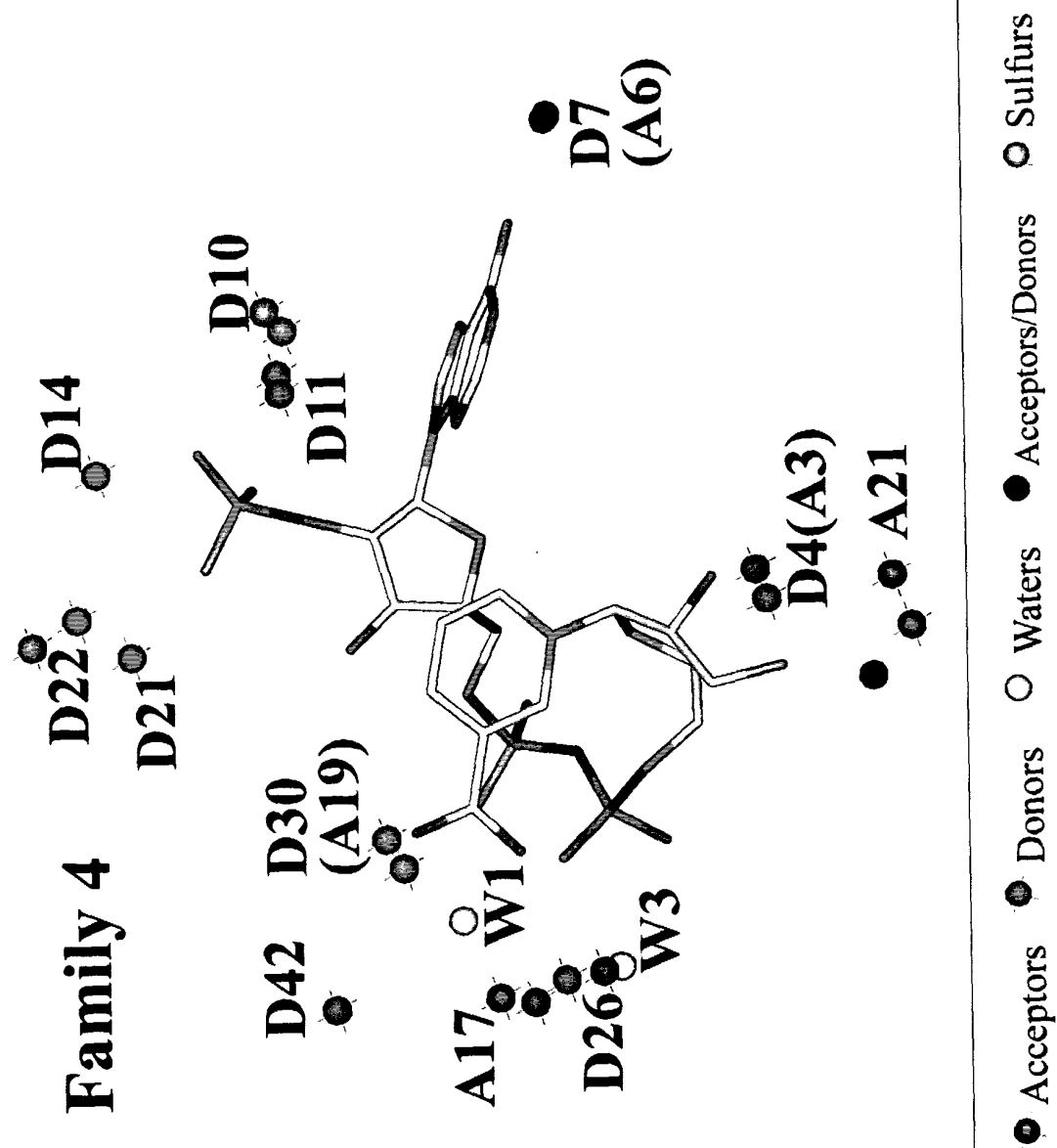
1004095 1301

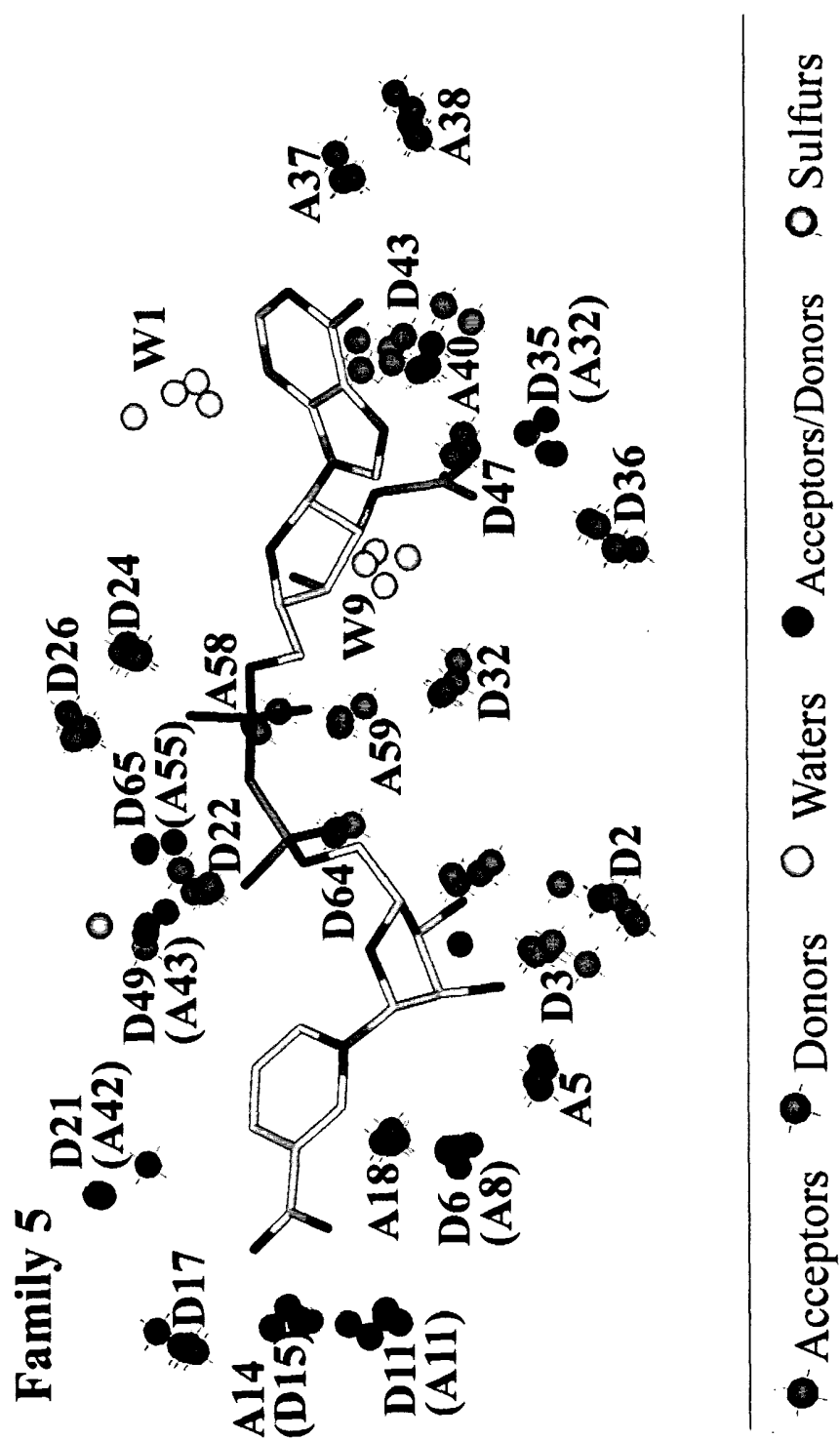


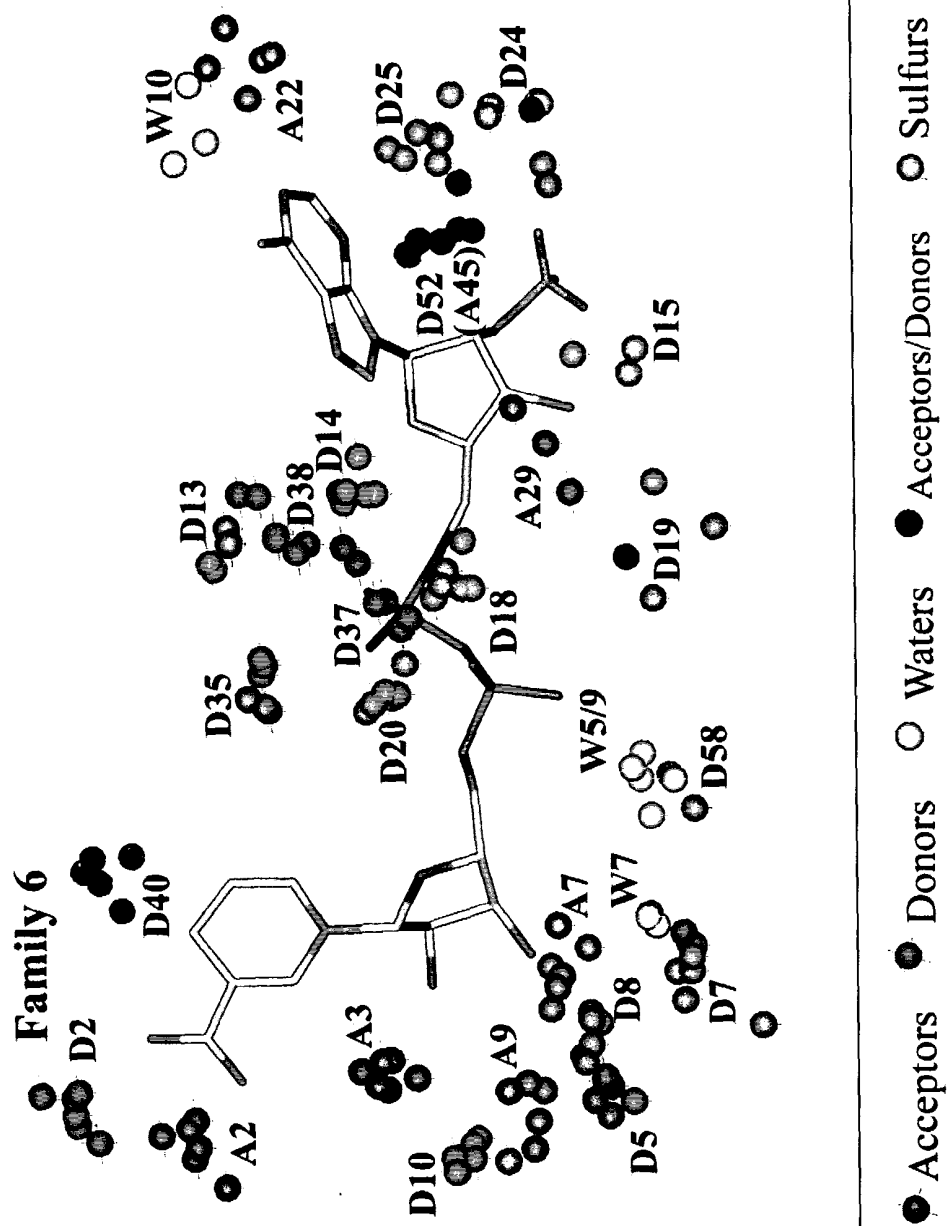


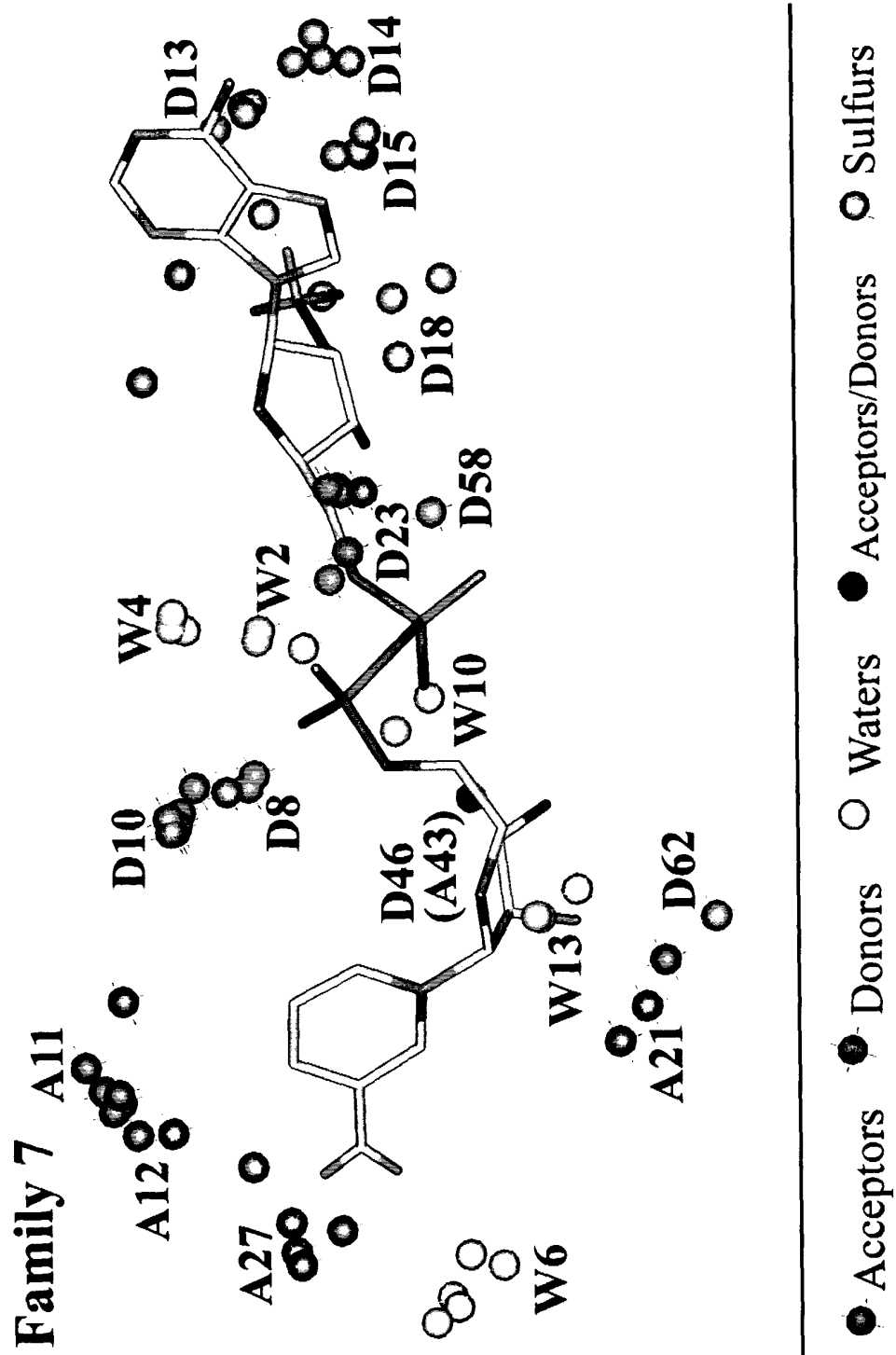
10



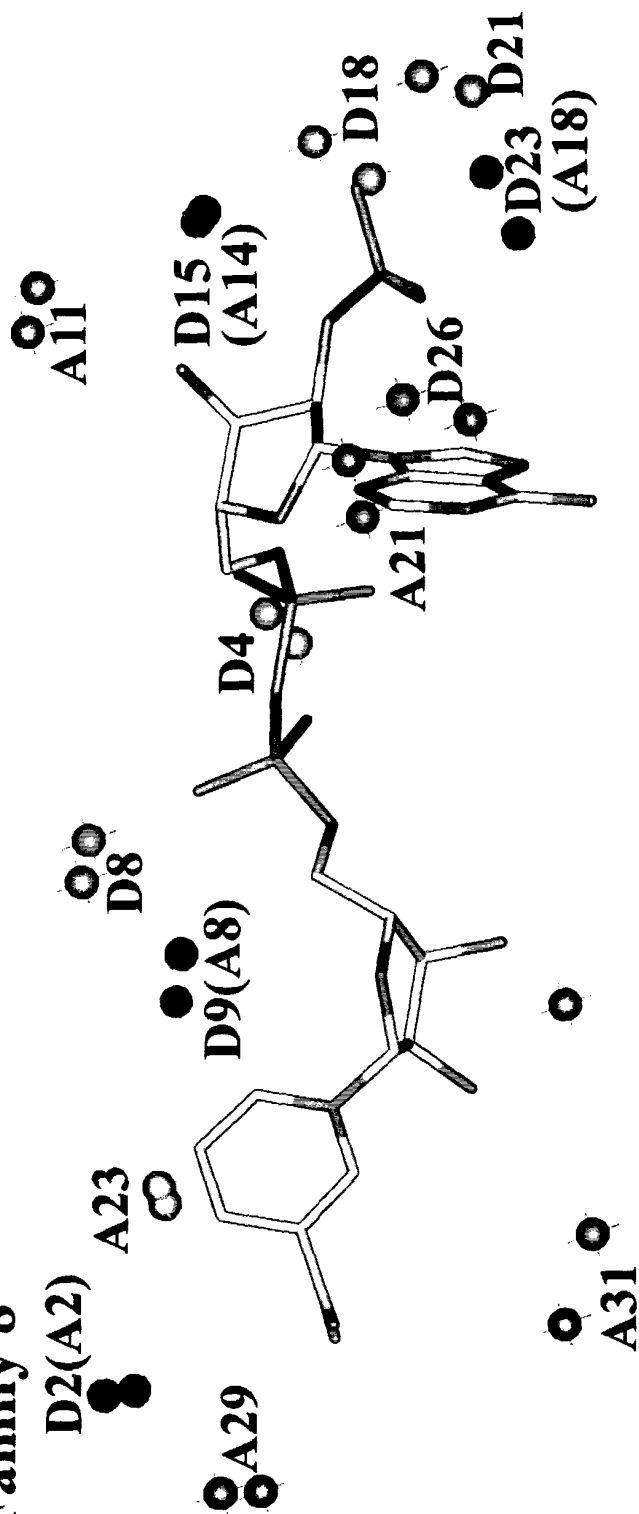




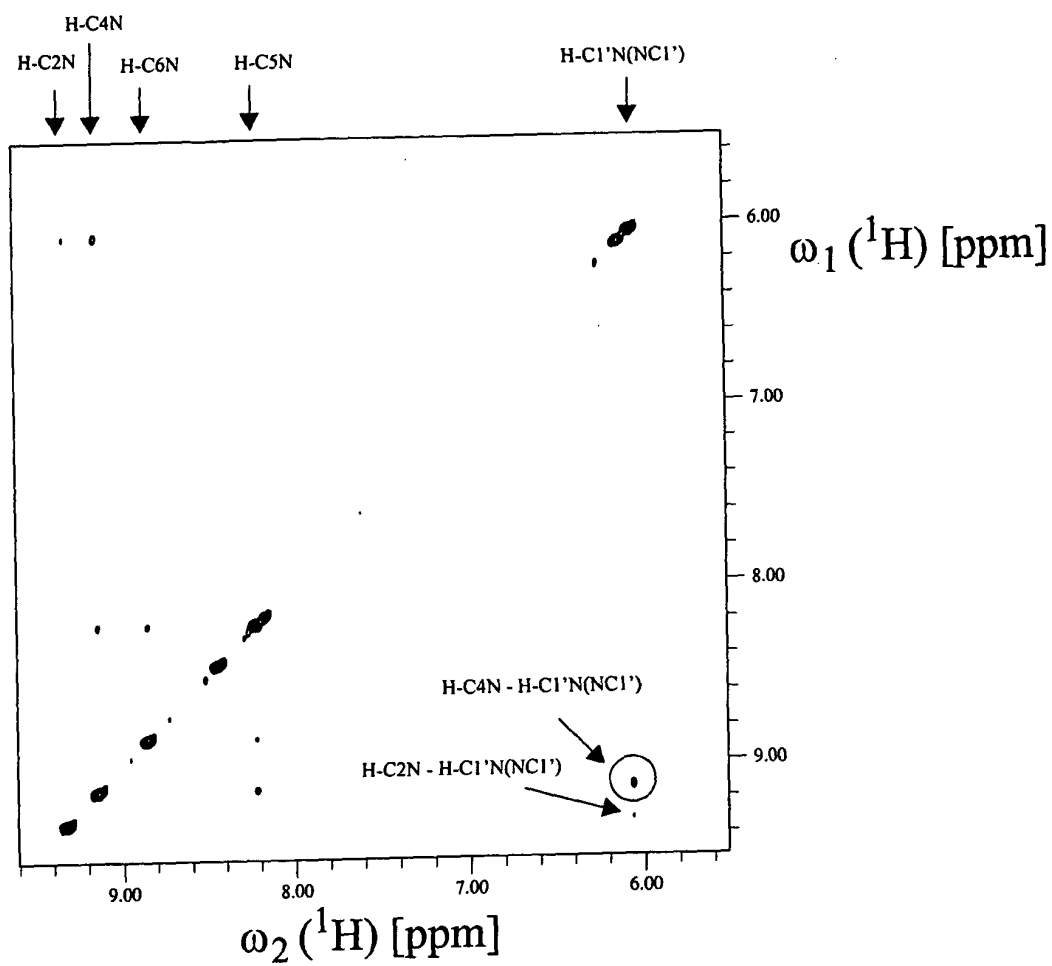




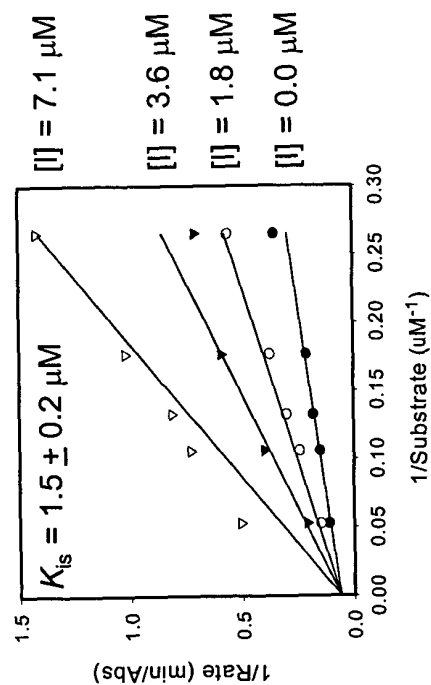
Family 8



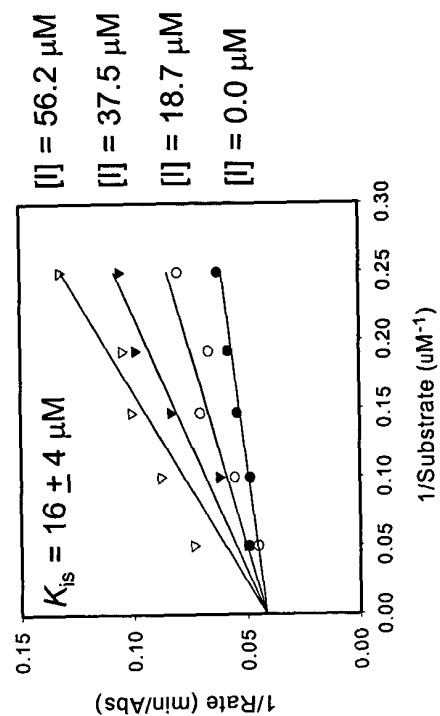
● Acceptors ● Donors ○ Waters ● Acceptors/Donors ○ Sulfurs



A.
Compound: TTE0001.001.A7
Pharmacofamily 1 exemplar

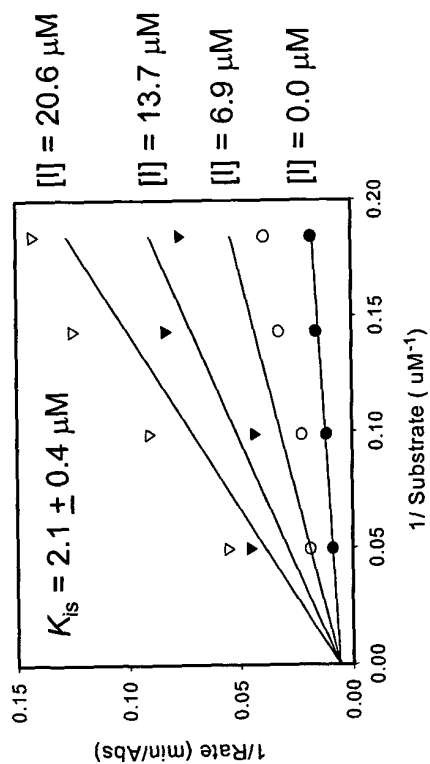


B.
Compound: TTE0001.001.A7
Pharmacofamily 8 exemplar



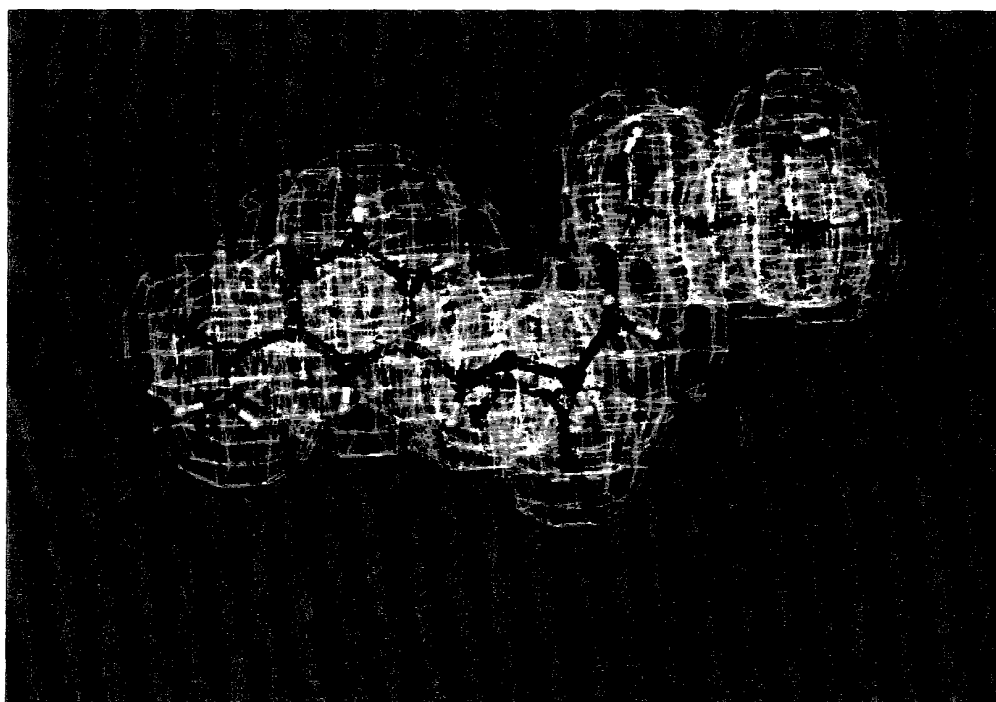
B.
Compound: TTE0001.002.D2
Pharmacofamily 8 exemplar

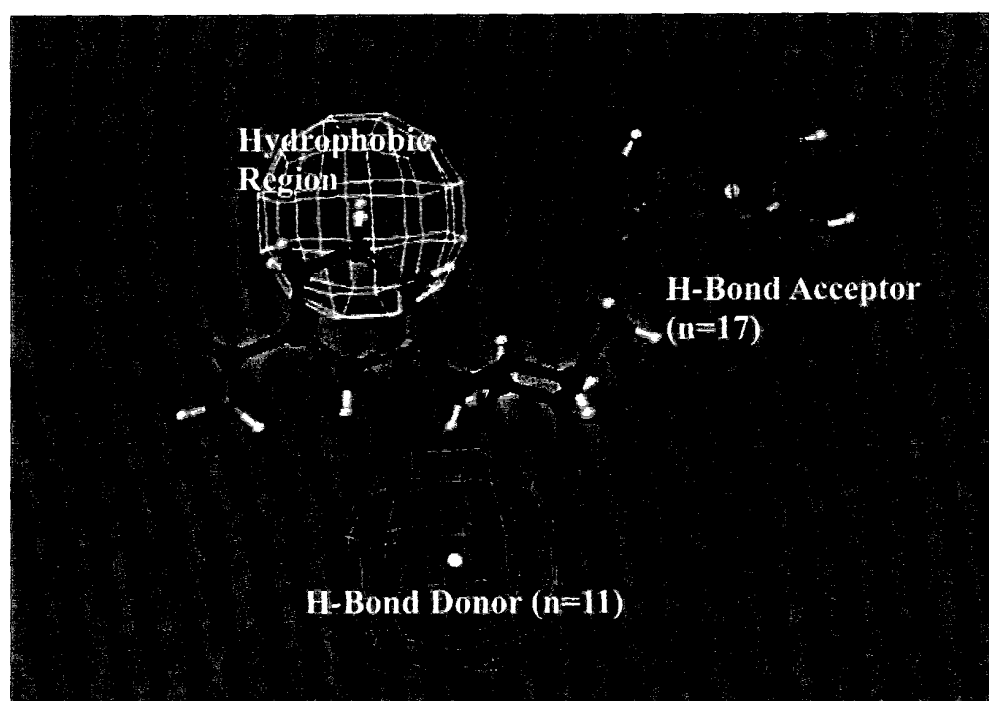
A.
Compound: TTE0001.002.D2
Pharmacofamily 1 exemplar



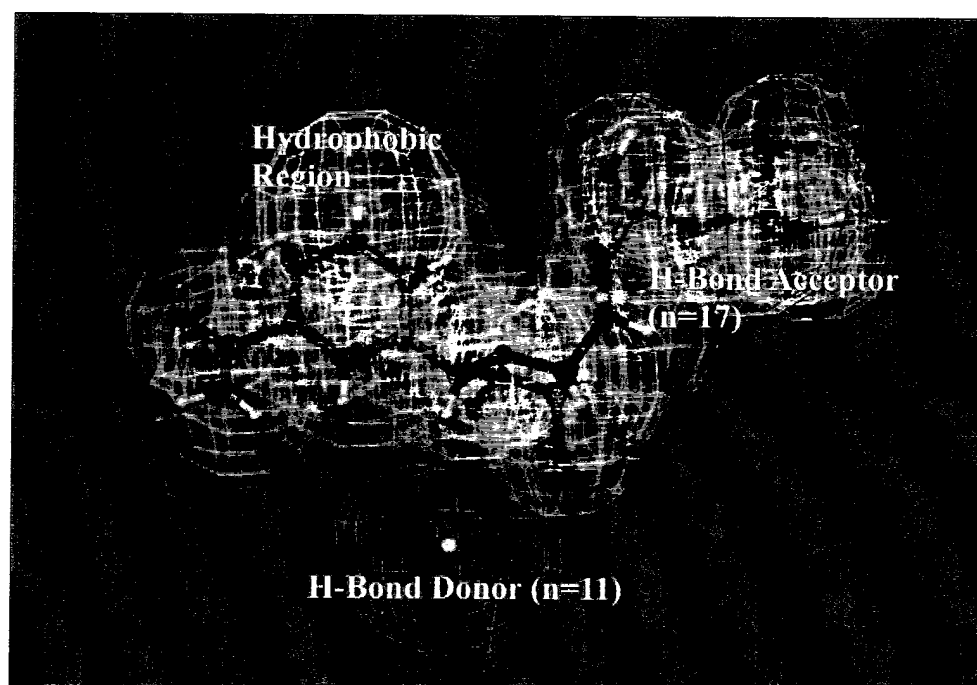
$K_{is} > 1 \text{ mM}$

10040600T 5680400T



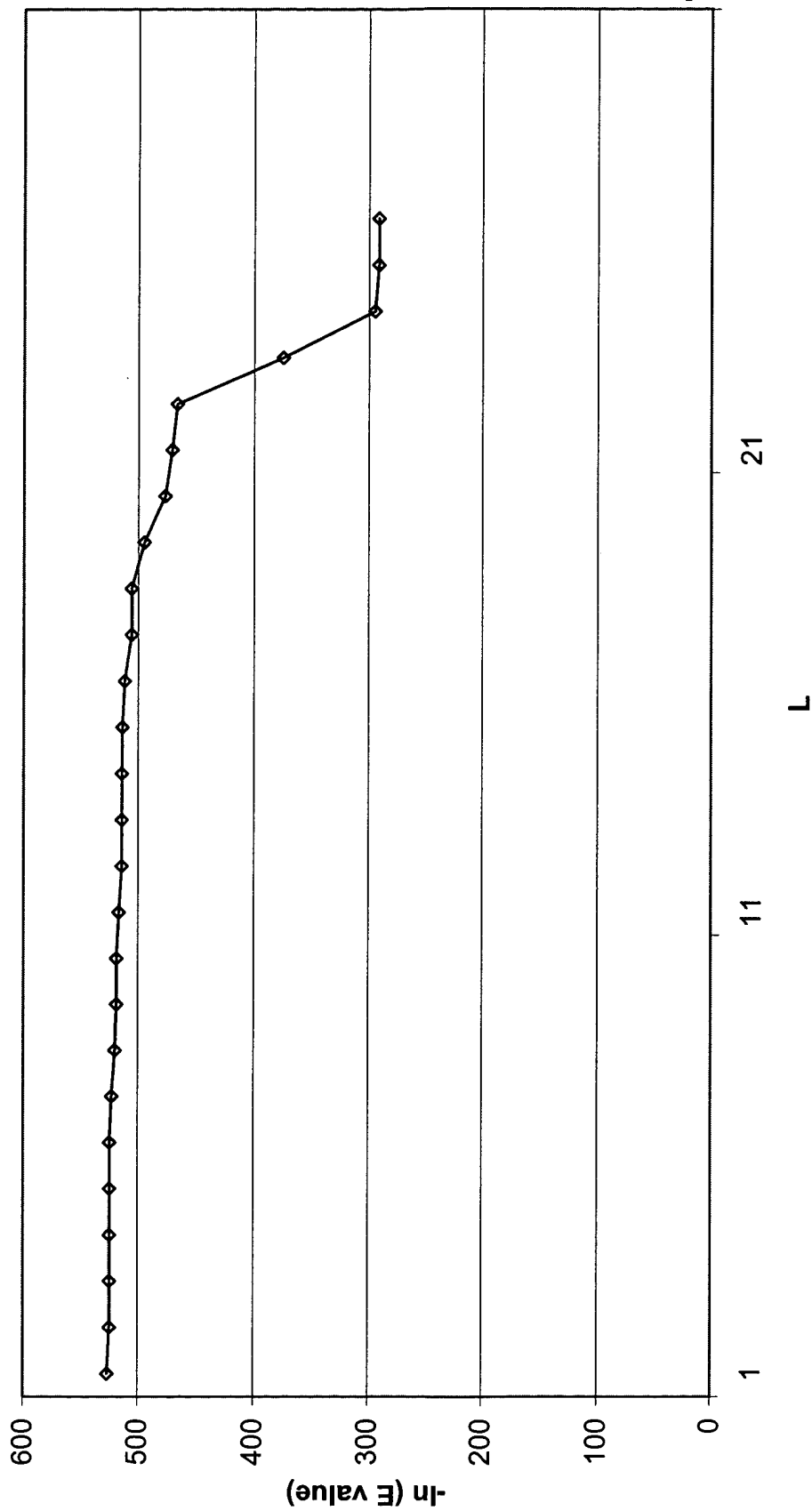


10040395-12401
T0322T " 5690400T



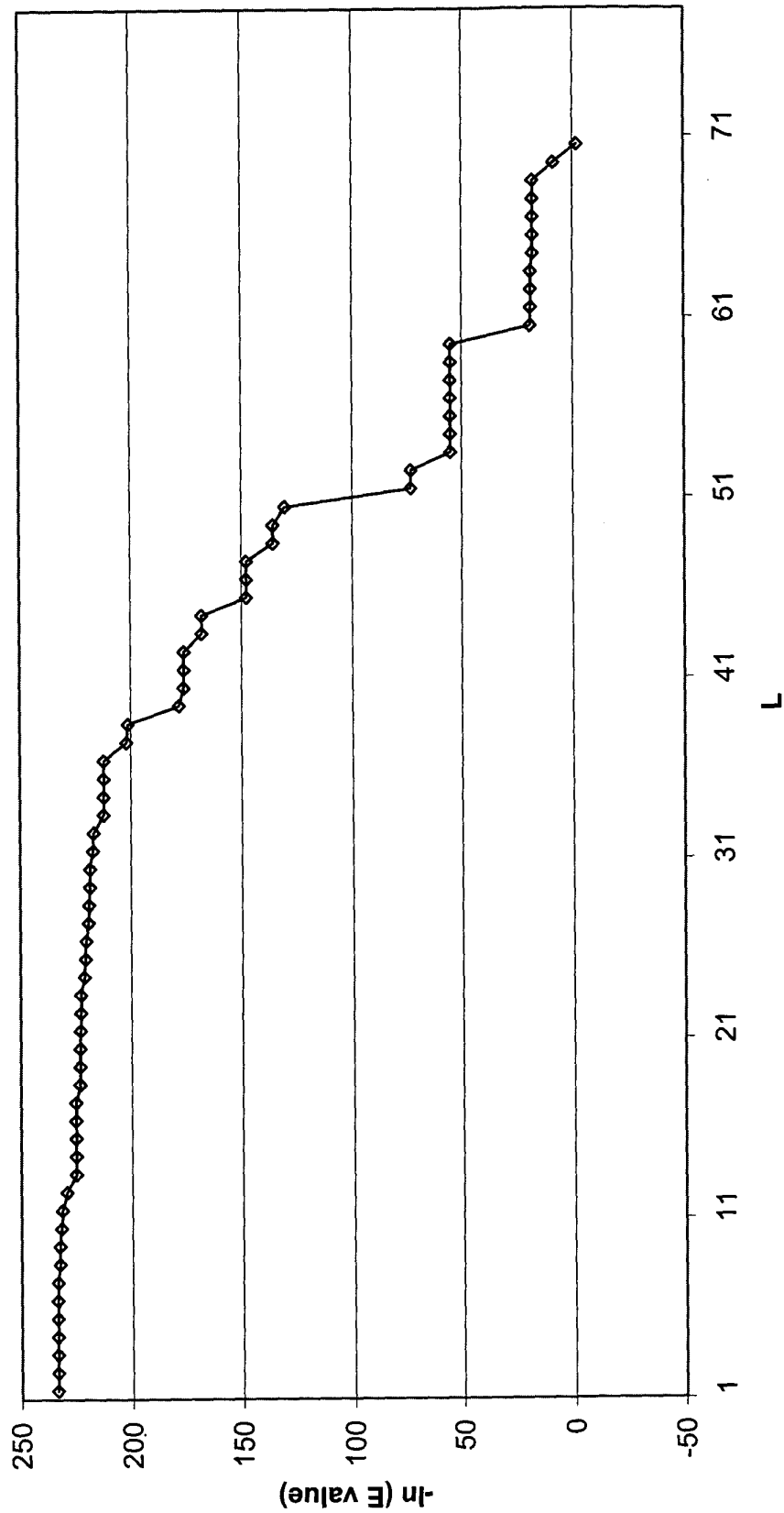
10040895-12301
T0222T-5680400T

Pharmacofamily 5



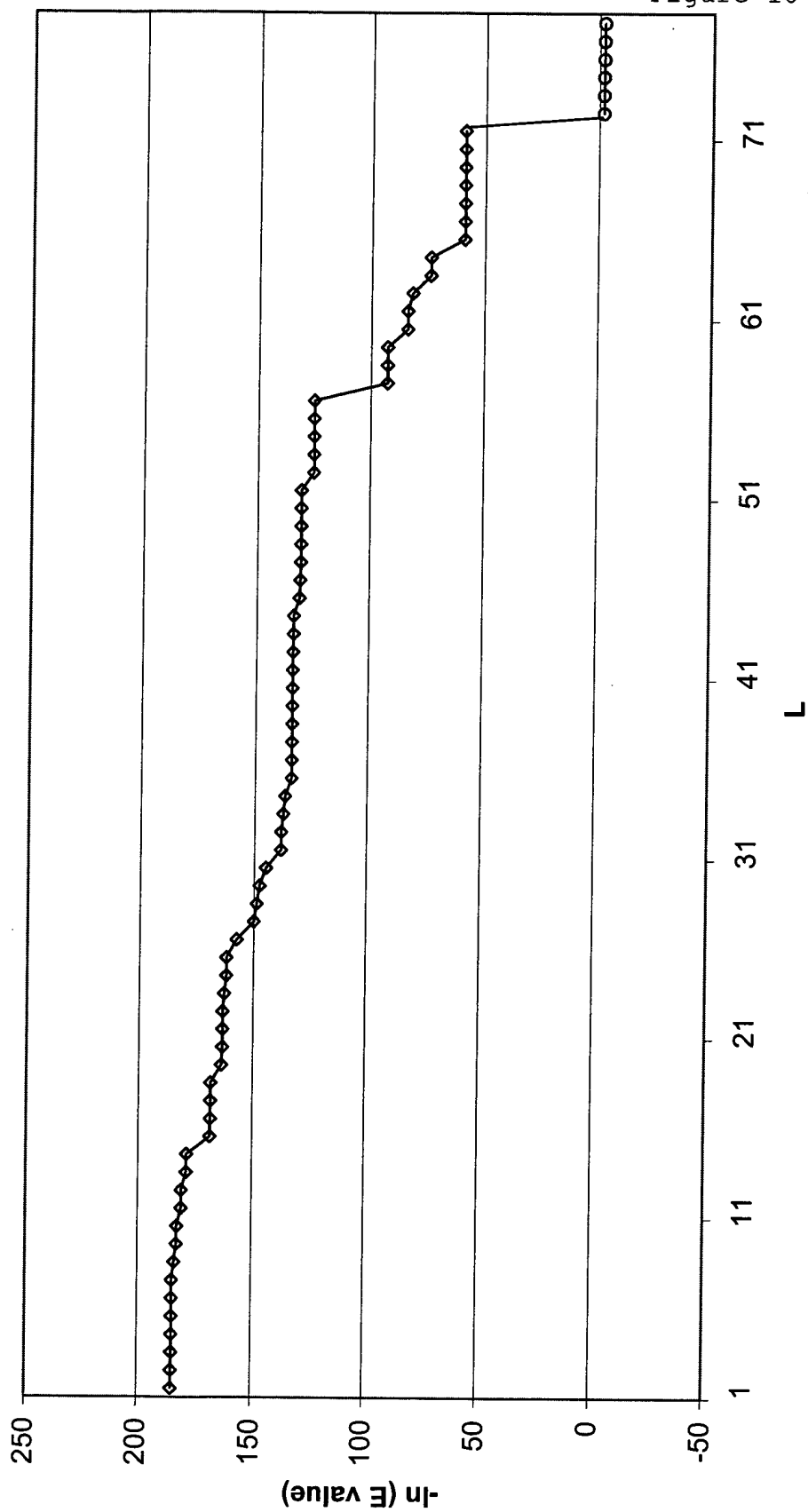
TEST "5690400T"

Pharmacofamily 3 : Training Set 1



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Figure 9

Pharmacofamily3 : Training Set 2



refinement cycle 5
profile center:1AGN
profile length: 599
1AGN
1AXE
1YKF
1HYH
1LDN
1EMD
9LDB
4MDH
1BMD
1PSD
1DXY
2NAD
1A4I
1B3R
1PJC
1ARZ
1QR6

1AGN:CL.....	IGC.	.GFSTGYGAA	VKTGK...V.
1AXE:	GC.	.GFSTGYGSA	VKVAK...V.
1YKF:VM.....	IPD.	.MMTTGFHGA	E.LAD...I.
1HYH:
1LDN:
1EMD:
9LDB:ATLKDQL.	I.HNL...L.
4MDH:
1BMD:
1PSD:P.....	.F.....	SN.	.TRSV AELV.	IGELL.LLLR
1DXY:	...SNV...	.P.....	AYS.	.PAAIAEFA.	LTDTL.YLLR
2NAD:	CN.	.SISVAEHV.	VMMIL.SLVR
1A4I:PCTPKGC.	LELIK.ET.G
1B3R:	KFD.	.NLYGCRESL.	IDGIKRAT.D
1PJC:	TPM	.SI.IAGRLSV	Q.FGA.RFLE
1ARZ:
1QR6:	LIQFEDFGNH	NAFRFLRK YR	EKYCTFNDD.IQGTAAVA.	LAGLL.AAQK

1AGN:	KP.....	.G.STCVVF.
1AXE:	TQ.....	.G.STCAVF.
1YKF:	EL.....	.G.ATVAVL.
1HYH:A.RKIGIIG
1LDN:	MK..NN	GG.ARVVVIG
1EMD:MKVAVLG
9LDB:KEE...HV	PH.NKITVVG
4MDH:SE.....	.P.IRVLVTG
1BMD:MKA.....	.P.VRVAVTG
1PSD:	..GVPEANAK	A..HRGV.W.	NKL..AA.G.	SFEAR.....G.KKLGII.
1DXY:	..NMGKVQAQ	L..QAGDYEK	AGT..F..I.	GKELG.....Q.QTVGVM.
2NAD:	..NYLPSHE.	WARK.GGWN.	.IADCVSHA.	Y.DLE.....A.MHVGTV.
1A4I:VPIA.....	.G.RHAVVV.
1B3R:VMIA.....	.G.KVAVVA.
1PJC:	RQQ.....	GGR	GVLLGGVPGV	KP.GKVVIL.
1ARZ:N.....	...IRVAIAG
1QR6:	..V.....	I.	SKP.I.....	.SEHKILFL.

T0322T " 568400T

1AGN: GLGG.VGLSV IMGCK..SA.G... .A.SRIIGID ..L.N.....
1AXE: GLGG.VGLSV IMGCK..AA.G... .A.ARIIGVD ..I.N.....
1YKF: GIGP.VGLMA VAGAK..LR.G... .A.GRIIAGVS.....
1HYH: L.GN.VGAAV AHGLIAQGV. .A..... .D..DYVFID A.N.E.....
1LDN: A.GF.VGASY VFALMNQGI. .A..... .D..EIVLID A.N.E.....
1EMD: AAGG.IGQAL ALLLKTQLP. .S...G... .S..ELSLYD I.A.P.....
9LDB: V.GA.VGMAC AISILMKEL. .A..... .D..EIALVD V.M.E.....
4MDH: AAGQ.IAYSL LYSIG.NG.S VFGKDQP... .I..ILVLLD ITP.MM....
1BMD: AAGQ.IGYSL LFRIA.AG.E MLGKDQP... .V..ILQLLE I.POAM....
1PSD: GYGH.IGTQL GILAE..SL.G... .M..YVYFYD I...E.....
1DXY: GTGH.IGQVA IKLFK..GF.G... .A..KVIAVD P...Y.....
2NAD: AAGR.IGLAV LRRILA..PF.D... .V..HLHYTDR.....
1A4I: GRSKIVGAPM HDLLL..WN.N... .A..TVTTCH S...K.....
1B3R: GYGD.VGKGC AQALR..GF.G... .A..RVIITE I...D.....
1PJC: GGGV.VGTEA AKMAV..GL.G... .A..QVQIFD I...N.....
1ARZ: AGGR.MGRQL IQAAL.ALE. GV..... .Q..LGAALF REG.SS....
1QR6: GAGE.AALGI ANLI...VS. ..VENGLSEQ EAQKKIW.FD K...YGLLVK

1AGN: ...KD.KFEK AM.AVGA... ..T.E.C...I
1AXE: ...KD.KFAK AK.EVGA... ..T.E.C...V
1YKF: ...RPVCVDA AK.YYGA... ..T.D.I...V
1HYH: ...A..KVK. .A.D.QID.. FQ.....DAM ANL.EAH.G. NI.V.I...N
1LDN: ...S..KAI. .G.D.AMD.. FN.....HGK V.FAPKP.V. DI.W.H...G
1EMD: ...V...TP. .G.V.AVD.. LS.....HI. .P..TA.V. KI.K.G...F
9LDB: ...D..KLK. .G.E.MMD.. LQ.....HGS L.F..LR.TP KI.V.S...G
4MDH: ...G..VLD. .G.V.LME.. L.....QDC ..A..LPPLK DV.I.A...T
1BMD: ...K..ALE. .G.V.VME.. LE.....DCAFPLLA GL.E.A...T
1PSD: ...N..K... .L...P.... LG..... NA.T.Q...V
1DXY:P... .M.K.GD... HP..... DF.D.Y...V
2NAD: ...H..R... .L.P..ES.. VE.....KE..L. NL.T.W...H
1A4I:
1B3R: ...PI.NAL..Q.A.AM... EG..... .Y.E.V...T
1PJC: ...VERL... .SYL..ETL. FG.....SRV.ELL...Y
1ARZ: ...L...LG. .S.D.A.... GELAGAGK.TGV.T.V...Q
1QR6: GRKAK..... .I.D...SYQ EP..... .FTHSAPESI

1AGN: S...PKDSTK PI.S.EVLSE M.T..G.NNV GYTFEVIG.. ...H.....
1AXE: N...PQDYKK PI.Q.EVLTE M.S..N.GGV DFSFEVIG.. ...R.....
1YKF: N...YKDG..PI.E.SQIMN L.T..EGKGV DAIIIAGG.. ...N.....
1HYH:D..... .W....A. .ALAD...A DVVISTLG.. ...NIKLQO..
1LDN:D..... .Y....D. .DCRD...A DLVVICAG.. ...AN..QKP
1EMD: SGE.D..... .A.T.PAL.. .E.G...A DVVLISAG.. ...VR..RK..
9LDB: K...D..... .Y..NVT.. .A.N...S RLVVITAG.. ...AR..QOE
4MDH: D...K..... .EEI..AFK. .D.....L DVAILVGS.. ...MP..RR..
1BMD: D.D.P..... .D.V..AFK. .D.....A DYALLVGA.. ...AP.RKA..
1PSD: Q.H.L..... .S.D..LLN. .M.....S DVVSLHVPEN .PST.....
1DXY: S...L..... .E.D..LFK. .Q.....S DVIDLHVPGI .EQN.....
2NAD: AT..R..... .E.D..MYP. .V.....C DVVTLNCPLH .PET.....
1A4I: TAH..L..... .D.E..EVN. .K.....G DILVVATG.. ...Q.....
1B3R: T...M..... .D.E..ACK. .E.....G NIFVTTG.. ...C.....
1PJC: SNSAE..... IE.T..AVA. .E.....A DLLIGAVLVP GRRRA.....
1ARZ: S...S..... .LDAV.K. .D.D...F DVFIDFT... ..R.....
1QR6: PDT.F..... ED.A...VN. ILK.....P STIIGVAGA.. ...G.....

1004095-12201

1AGN:L...ETM .I.DALA.SCHMNYGT SVVVGV..P.
1AXE:L...DTM .V.TALS.CCQEAYGV SVIVGV..P.
1YKF:A...DIM .A.TAVK.IVKPGGT IANVNY..F.
1HYH:FA...E LKFTSSMV.Q S...V.GTNLK .ESGFH..GV LVVISN.P..
1LDN: GET.RLD..L VDKNIAIF.R S..I.VESVM .ASGFQ..GL FLVATN.P..
1EMD: PGMDRSD..L FNVNAGIV.K N..L.VQOVA .KT.CP.KAC IGIITN.P..
9LDB: G.ESRLN..L VQRNVNIF.K F..I.IPNIV .KY.SP.NCK LLVVSN.P..
4MDH: DGMERKDL.L .KANVKIF.K C..Q.GAALD .KY.AKKSVM VIVVSN.P..
1BMD: .GM..ERRDL LQVNGKIF.T E..Q.GRALA .EV.AKKDVK VLVVGN.P..
1PSD:K..NM.M GAKE.ISLM.KP.GSL LINASR.GT.
1DXY:T..HI..I NEAA.FNLM.KP.GAI VINTAR.PN.
2NAD:E..HM.I NDET.LKLF.KR.GAY IVNTAR.GK.
1A4I:P..EM.V ...K.GEWI.KP.GAI VIDCGI..N.
1B3R:V...DII ...L.GRHFE .Q..MKDDAI VCNIGH.F..
1PJC:P...I.L ...VPASLVE .Q..MRTGSV IVDVAV.DO.
1ARZ:P..EGTL N..H.LAFCR .Q..HG..KG MVIGTT..G.
1QR6:R...L.F TPDV.IR..A AS..INERPV IFALSNPTAQ

1AGN: .PSA.K.M.. .L.TY.D.PML...L...FT..
1AXE: .PDS.Q.N.. .L.SM.N.PML...L...LS..
1YKF: .GE..GEV.. ...L...PVPRL EWGC..G...MA..
1HYH:V.D.. .V.I..TALFQHV..TG..
1LDN:V.D.. .I.L..TYATWKF..SG..
1EMD:V.N.. .T.T..VAIAAEV..LKKA
9LDB:V.D.. .I.L..TYVAWKI..SG..
4MDH:A.N.. .T.N..CLTASKS..AP..
1BMD:A.N.. .T.N..ALIAYKN..AP..
1PSD: .V...V.D.. .I.PA.LCDAL...A...SK..
1DXY: .L...I.D.. .T.QA.MLSNL...K...SG..
2NAD: .L...C.D.. .R.DA.VARAL...E...SG..
1A4I: ..YKVV.G.. .D.VA.YD.EA... .K...E...
1B3R:D.V.. .E.ID.VKW.LNEN. ...AVEKVNI KPQVDRL..
1PJC:G.. .GCVETLHPT SHTQPTY... .E...V...
1ARZ:F.DEA GK.QA.IRDAA.....AD..
1QR6: AE...C.... .TAE.E.AYTLT...E...

1AGN:GR.T WK.....GC
1AXE:GR.T WK.....GA
1YKF:HK.T IK.....GG
1HYH:FPAHK VI..G...TGT.....
1LDN:LPHER VI..G...S.....
1EMD: GV...YDKNK LF..G...VTTL DI...IRSNT FVAEL..KGK
9LDB:FPKNR VI..G...SGC...N.....
4MDH: .S...IPKEN FS..C...LTRL DH...NRAKA QIALK..LGV
1BMD: .G...LNPRN FT..A...MTR.....
1PSD:H.LAG AA.....ID VFPTE...P..ATNSD....PF.T..S..
1DXY:K.LAG VG.....ID TYEYETEDL..LN..LAKH. GSFKDPLW.D
2NAD:R.LAG YA.....GD VWFPQ...P..A.....PK.D..H..
1A4I:R.ASF IT..PVPGGVG...P.....
1B3R: .LKNGHRI.I LLAEG...RL V...N...L.....
1PJC:FGV.V HY..G...VP
1ARZ:I.A IV..F...A.A..N.....
1QR6:GRC LF..A...SG SP..F.....G.P

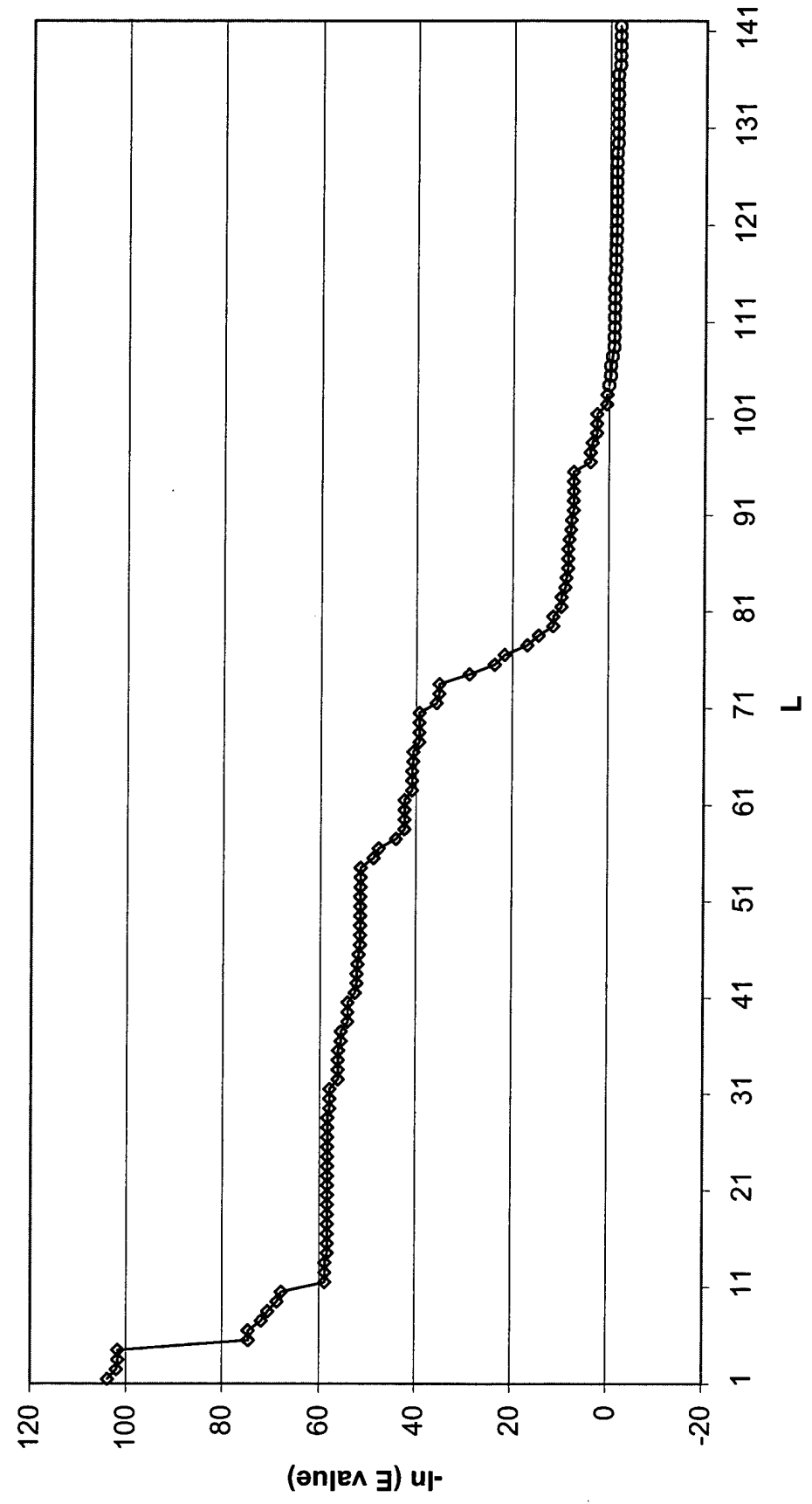
TABLE 1 " SEQUENCE

1AGN:	<u>V</u>	<u>F</u> GG.L...KS
1AXE:	<u>I</u>	<u>F</u> GG.F...KS
1YKF:	<u>L</u>	<u>C</u> ...P...GG	..RLRME...	R.LIDL....
1HYH:				
1LDN:				
1EMD:	QPGE....VE	V.PVIG. <u>GHS</u>	G.V.TI..LP	LLS.QVPG..	...V....SF
9LDB:				
4MDH:	TS.D....DV	KNVIIWGN <u>HS</u>	S.T.Q...YP	DVNHAKVKLQ	AKEVGVEAV
1BMD:	<u>LD</u>			
1PSD:	.P.L....CE	FDNVLLTP <u>HI</u>	<u>G</u> . <u>G</u> .S...TQ	EAQENI....
1DXY:	.E.L....LG	MPNVVLS <u>PHI</u>	<u>A</u> . <u>Y</u> .Y...TE	TAVHN <u>MV</u> ...	Y.FSLQ....
2NAD:	.P.W....RT	MPYNGMTP <u>HI</u>	S.G.T....		
1A4I:	M.	<u>TVA</u> .M...LM	.Q..S....	
1B3R:	G.C.	A. <u>MGH</u> ...PS	FV.....	
1PJC:	<u>NM</u>	<u>PGA</u> .VPWTA.		
1ARZ:	<u>F</u>	S.V.G...A.	.S..S....	
1QR6:	.V.KLTDGRV	F..TPG <u>QGN</u> .	<u>NVY</u> .I...FP	GVALAVILCN	TRHISD....
1AGN:				
1AXE:				
1YKF:V..FYKR	VDPS.K.L..
1HYH:				
1LDN:				
1EMD:	T.E.QEV.AD	LTKRIQNAG <u>T</u>	EV <u>VEAKAGGG</u>	<u>SATLSMGQAA</u>	ARFGLS.LVR
9LDB:				
4MDH:	KDDSW.LKGE	FITTVQQRGA	AVIKARK..L	SSAMSAAKAI	CDHV.RDI..
1BMD:				
1PSD:				
1DXY:	H.LVDFLTKG	ETSTEVTG..		
2NAD:				
1A4I:				
1B3R:				
1PJC:				
1ARZ: <u>R</u> ..MT <u>FA</u>	NGAV.RSAL.
1QR6:S..VFLE	<u>AA</u> ...KA...
1AGN:				
1AXE:				
1YKF:	V.			
1HYH:				
1LDN:				
1EMD:	A.LQGEQGVVECAYV	EG.DG..QYA	..RFFS.QPL	LLGKNGVEER
9LDB:				
4MDH:	W....F..GT	PEGEFVSMGI	ISDGNSYGV	DDLLYSFPVT	IKD..KT.WK
1BMD:				
1PSD:				
1DXY:				
2NAD:				
1A4I:				
1B3R:				
1PJC:				
1ARZ:	WLSGKESGLFDMR...		...D.	
1QR6:LT	S..QLTD...	EELA

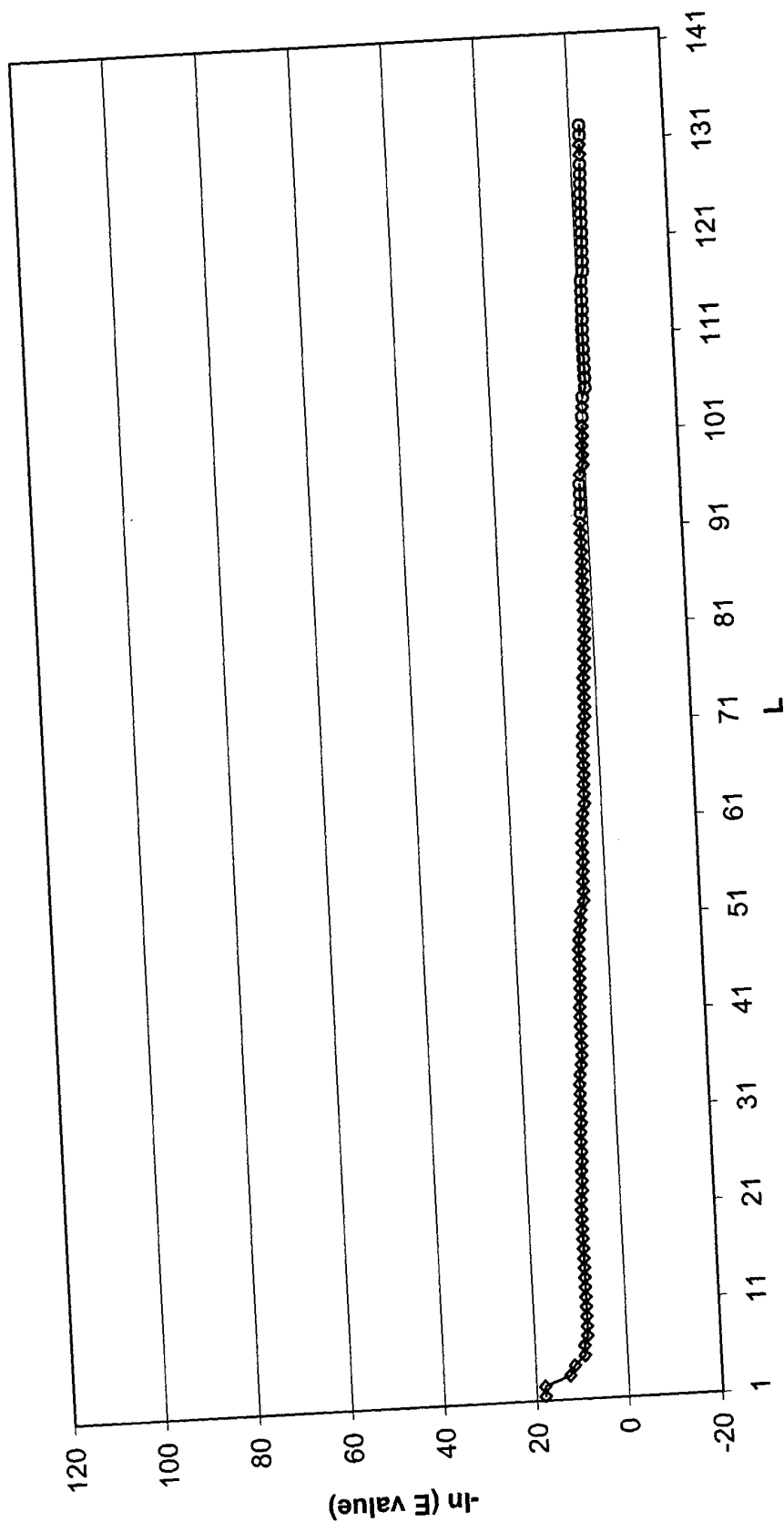
1AGN:
1AXE:
1YKF:
1HYH:
1LDN:
1EMD: K.S....I.G TLSAFEQNAL EG.ML...DT LKK.DIALGQ EF..VNK..
9LDB:
4MDH: I.V....EGL PI.N..DFS. REKMDLTAK L.AEE..KET AFEFL.SSA
1BMD:
1PSD:
1DXY:
2NAD:
1A4I:
1B3R:
1PJC:
1ARZ: ...VLDLN.N L.....
1QR6: QGRLYPPL.A NIQE.VSINI AIKVTEYLYA NKAFRYPEPE DKAKYVKER

FOSET "SEB0400T"

Pharmacofamily 1

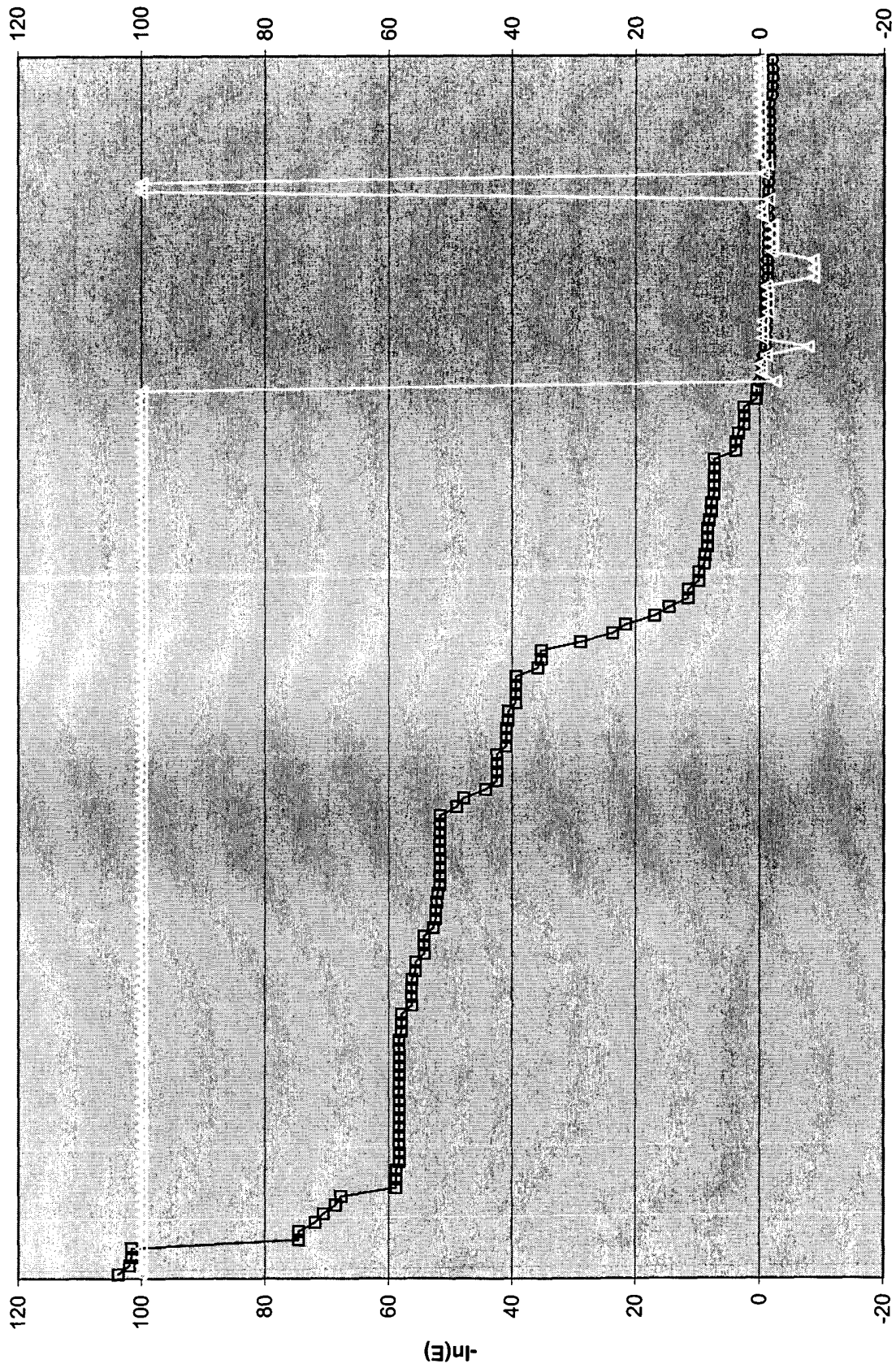


Pharmacofamily 1 with Differential Filtering



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Figure 14



PDB Proteins for Pharmacofamily 1